

## *REMARKS*

### *The Present Invention and Pending Claims*

Claims 1-14 and 27-38 are currently pending and directed to a liquid composition for maintaining a non-enveloped viral vector.

### *The Amendments to the Claims*

Claims 1-3 have been amended to point out more particularly and claim more distinctly the subject matter of the invention. Specifically, claim 1 has been amended to recite that the composition comprises about 0.05-1.5 mM of a divalent metal salt; claim 2 has been amended to recite that the composition comprises about 0.05-1 mM of a divalent metal salt; and claim 3 has been amended to recite that the composition comprises about 0.05-1 mM of magnesium chloride (MgCl<sub>2</sub>). These amendments are supported by the specification at, for example, paragraph [0011]. Claims 15-26 have been canceled as drawn to non-elected subject matter. Applicants reserve the right to pursue any canceled subject matter in a continuation, continuation-in-part, divisional application, or other application. Cancellation of any subject matter should not be construed as abandonment of that subject matter. New claims 27-38 represent other combinations of features already recited in claims 1-14. Accordingly, no new matter has been added by way of these amendments.

### *The Office Action*

The Office Action rejects the pending claims under 35 U.S.C. § 103(a) as allegedly encompassing obvious subject matter in view one or more of the following references: EP 0872249 A1 (Kuma et al.), US 5,792,643 (Herrmann et al.), US 2002/0041884 A1 (Evans et al.), WO 01/66137 (Evans et al.), WO 00/34444 (Kovesdi et al.), and WO 99/41416 (Frei et al.). The Office Action also rejects the pending claims under the judicially created doctrine of obviousness-type double patenting over claims 12-24 of US 6,514,943 (Kovesdi et al.) or claims 13-20 of US 6,225,289 (Kovesdi et al.) in view of the aforementioned Evans references.

### *Discussion of the Obviousness Rejections*

The claims, as amended, are directed to a composition for maintaining a non-enveloped viral vector comprising (a) about 1-25% (wt./vol.) trehalose, (b) about 0.05-1.5 mM of a divalent metal salt, (c) a multiplicity of non-enveloped viral vector particles, and (d) a liquid carrier.

The Kuma reference does not teach or suggest a composition comprising a divalent metal salt, much less a divalent metal salt in a concentration of about 0.05-1.5 mM, as recited in the pending claims. Since the Kuma reference does not disclose, nor suggest, all of the elements of the pending claims, the Kuma reference cannot itself properly form the basis of a *prima facie* obviousness rejection.

While the Herrmann reference discloses the addition of a “neutral salt” which can be sodium chloride, potassium chloride, or magnesium chloride (see col. 7, lines 4-6, of US 5,792,643), there is no teaching or suggestion within the Herrmann reference to use about 0.05-1.5 mM of a divalent metal salt as required by the pending claims. Similarly, the Evans references disclose a composition comprising a divalent cation (e.g.,  $\text{MgCl}_2$ ) at a concentration of about 0.1-10 mM, with a preferred range of about 0.1-5 mM (see paragraphs [0052] and [0070] of US 2002/0041884 A1, and page 9, lines 8-9, of WO 01/66137), but the Evans references do not contain any teaching or suggestion to use about 0.05-1.5 mM of a divalent metal salt as required by the pending claims. The Kovesdi reference discloses compositions containing 10 mM  $\text{MgCl}_2$  (see page 11, lines 20-24, of WO 00/34444); however, the Kovesdi reference does not disclose or suggest the use of about 0.05-1.5 mM of a divalent metal salt as required by the pending claims. While the Frei reference discloses compositions that include 0.1-1 mg/ml of a divalent metal salt (which is equivalent to about 1-10 mM  $\text{MgCl}_2$ ), and most preferably 0.4 mg/ml of a divalent metal salt (which is equivalent to about 4 mM  $\text{MgCl}_2$ ) (see page 5, lines 31-35, of WO 99/41416), the Frei reference does not contain any teaching or suggestion to use about 0.05-1.5 mM of a divalent metal salt as required by the pending claims.

The claims of the Kovesdi ‘943 and ‘289 patents relied upon to support the obviousness-type double patenting rejections are no more relevant inasmuch as the identified claims do not teach or suggest the use of about 0.05-1.5 mM of a divalent metal salt as required by the pending claims.

Thus, none of the cited references teaches or suggests the particular amount of a divalent metal salt required by the pending claims, let alone in the context of the claimed non-enveloped viral vector preservation composition that also contains trehalose, non-enveloped viral vector particles, and a liquid carrier. As described in the accompanying Rule 132 Declaration, Applicants unexpectedly discovered that the inclusion in a non-enveloped viral vector preservation composition of a divalent metal salt (e.g.,  $\text{MgCl}_2$ ) in a concentration of about 0.05-1.5 mM greatly improved the stability of the viral vectors of the composition relative to compositions containing larger amounts of a divalent metal salt.


In re Appln. of Kovesdi et al.  
Application No. 10/046,517

In the absence of a teaching or suggestion directing one of ordinary skill in the art to modify the disclosure of any of the cited references so as to use about 0.5-1.5 mM of a divalent metal salt in a non-enveloped viral vector composition comprising trehalose, non-enveloped viral vector particles, and a liquid carrier, the composition recited in the pending claims must be considered unobvious in view of the cited references.

*Conclusion*

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

  
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Amendment or ROA - Final (Revised 7/29/03)